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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,992	06/09/2005	Hiroshi Matsui	081356-0243	1370

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EXAMINER	
MARTIN, PAUL C	

ART UNIT	PAPER NUMBER
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,992	MATSUI, HIROSHI	
	Examiner	Art Unit	
	PAUL C. MARTIN	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 13-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 13-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1 and 13-24 are pending in this application and were examined on their merits.

The rejection of pending Claims 1, 13-15, 20 and 21 as conflicting with Claims 1-5 and 7-13 of co-pending Application 10/594,898 has been withdrawn because the Applicant's arguments filed 12/13/07 regarding the separate measurements of generated compounds was found to be persuasive.

The rejection of Claims 1, 13 20, 21 and 22 under 35 U.S.C. § 102(b) as being anticipated by Nakamura *et al.* (US 6,333,166 B1) has been withdrawn because the Applicant's arguments filed 12/13/07 regarding the single measurement of a generated compound vs. the instant dual measurements of a generated compound were found to be persuasive.

The rejection of Claims 25 and 27-29 under 35 U.S.C. § 103(a) as being unpatentable over Matsui *et al.* (US 6,194,164 B1) has been withdrawn due to the Applicant's cancellation of the Claims filed 12/13/07.

The rejection of Claims 25-29 under 35 U.S.C. § 103(a) as being unpatentable over Matsui *et al.* (US 6,194,164 B1) has been withdrawn due to the Applicant's cancellation of the Claims filed 12/13/07.

The rejection of Claims 1, 13-16 and 19-22 under 35 U.S.C. § 103(a) as being unpatentable over Nakamura *et al.* (US 6,333,166 B1) in view of Matsui *et al.* (US 6,194,164 B1) has been withdrawn because the Applicant's arguments filed 12/13/07 regarding the separate measurements of generated compounds was found to be persuasive.

The rejection of Claims 1, 13, 17, 18, 20, 21 and 22 under 35 U.S.C. § 103(a) as being unpatentable over Nakamura *et al.* (US 6,333,166 B1) in view of Sugiuchi *et al.* (US 6,794,157 B1) has been withdrawn because the Applicant's arguments filed 12/13/07 regarding the separate measurements of generated compounds was found to be persuasive.

The rejection of Claims 1, 13, 20, 21, 22, 23 and 24 under 35 U.S.C. § 103(a) as being unpatentable over Nakamura *et al.* (US 6,333,166 B1) in view of Kishi *et al.* (US 2003/0129681 A1) has been withdrawn because the Applicant's arguments filed 12/13/07 regarding the separate measurements of generated compounds was found to be persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 13-24 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The method of Claim 1 relies upon introducing to a sample a reagent that acts on the cholesterol in lipoproteins other than low density lipoprotein (LDL) to generate a compound and measuring the absorbance of the compound, then further introducing to the sample a second reagent that acts on at least the LDL to generate an additional amount of the same compound generated in the first step and then measuring the elevated absorbance of the compound. The fact that the method relies upon the generation of the same compound in both reagent addition steps requires that the enzyme reactions in at least the first reaction step be run to completion before measuring the absorbance.

It cannot be conclusively determined from the disclosure that the first reaction step is run to completion, (i.e., that the other than LDL cholesterol derived compound has been fully converted or generated to completion). If the first reaction is not run to completion, the difference between the measured values from the first and second steps will not result in an accurate measure of either the total cholesterol or the LDL cholesterol. It is noted that the examples only require a total reaction time of the first reagent on cholesterol other than LDL of 5 minutes for both the experimental and control reactions however the experimental data does not indicate graphically that the reaction is fully completed by 5 minutes. Further, the method requires the use of a first reagent comprising a surfactant that acts only on lipoproteins other than the LDL and a second reagent comprising a surfactant that acts on at least the LDL lipoproteins. The Specification indicates that the surfactant of the first step is also an unspecified polyalkylene oxide derivative having and HLB value of having an HLB value of $13 \leq X \leq 15$ and preferably having an HLB value of $13 \leq X \leq 14$ (Specification, Pg. 12, Lines 7-9). The surfactant capable of acting selectively on LDL *or a surfactant that acts on all lipoproteins* is an unspecified polyalkylene oxide derivative that in a preferred embodiment acts on all lipoproteins and has an HLD value of $11 \leq X \leq 13$ and preferably has an HLB value of $12 \leq X \leq 13$ (Specification, Pg. 15, Lines 6-18). The Specification seems to teach that the surfactants of both the first and second reagents can both be capable of acting non-selectively on all lipoproteins. In this case, such non-specificity would render impossible a determination of the separate values of measurements from lipoproteins other than LDL and LDL solely.

Further, the Specification teaches that both surfactants even in the preferred embodiments have HLB values that at least are capable of overlapping at the HLB value of 13. In this case, the requisite specificity of the surfactants for enabling the reagents to act on lipoproteins other than LDL and only on LDL would not exist and the method would not yield the desired results. For these reasons, the Examiner has determined that the method as claimed is not sufficiently enabled by the Disclosure so that one of ordinary skill in the art would be able to use the invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 13-24 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 requires the use of a first reagent that acts on the cholesterol on lipoproteins to generate a compound and a second reagent that acts on at least the LDL lipoprotein to generate an additional amount of said compound. The term "acts" is undefined in the Specification such that it cannot be determined what is meant by the term and by what mechanism the compound is therefore generated.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 13-15 and 20-22 are newly rejected under 35 U.S.C. 102(e) as being anticipated by Shull *et al.* (US 2004/0126830 A1).

Shull *et al.* teaches a method for measuring on one assay, total cholesterol and low density lipoprotein (LDL) cholesterol in whole blood or plasma the method comprising, applying a whole blood sample to a test strip stack comprising a reagent containing cholesterol esterase, cholesterol oxidase, peroxidase, 4-amino antipyrine, bovine serum albumin, the colored quinone MAOS and a surfactant that acts on the cholesterol in lipoproteins other than LDL to generate a colored compound measuring the absorbance with an automated analyzer, and applying a whole blood sample to a test strip comprising a second reagent comprising a surfactant that acts on at least the LDL to generate additional amounts of the same colored compound and measuring the absorbance with an automated analyzer and wherein the value of LDL cholesterol was calculated as the difference between the total cholesterol and the Non-LDL cholesterol (Pg. 6, Paragraphs [0069]-[0072]).

The Examiner has interpreted that the steps of introducing in said sample a first reagent and a second reagent as being inherently present in the method of Shull *et al.* because the same sample is introduced to test strips that contain the reagents. The Claimed invention does not specify that the same sample which is introduced to the first reagent must also be introduced to the second reagent sequentially.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 13-16 and 19-22 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Shull *et al.* (US 2004/0126830 A1) in view of Matsui *et al.* (US 6,194,164 B1).

The teachings of Shull *et al.* were discussed above.

Shull *et al.* does not teach a method wherein the cholesterol esterase is produced by bacterial *Pseudomonas*.

Matsui *et al.* teaches a method for quantifying LDL cholesterol wherein the cholesterol esterase is preferably originated from *Pseudomonas* (Column 3, Line 3-7).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Shull *et al.* to use cholesterol esterase from *Pseudomonas* as taught by Matsui *et al.* because it is *prima facie* obvious to select a known material based on its suitability for its intended purpose. The MPEP states:

> The selection of a known material based on its suitability for its intended use supported a prima facie obviousness determination in *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945).

In this case the selection of a cholesterol esterase from bacteria would have been desirable because bacteria are easily propagated in large numbers and would yield correspondingly large amounts of the desired enzyme for experimental use. There would have been a reasonable expectation of success in making this substitution because both methods utilize cholesterol esterase in similar methods of quantifying LDL.

Claims 1, 13-15, 17, 18 and 20-22 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Shull *et al.* (US 2004/0126830 A1) in view of Sugiuchi (US 6,794,157 B1).

The teachings of Shull *et al.* were discussed above.

Shull *et al.* does not teach a method wherein the first reagent comprises a surfactant that acts only on lipoproteins other than LDL, cholesterol esterase and cholesterol dehydrogenase, and wherein the generated compound is reduced β-nicotinamide adenine dinucleotide (NADH).

Sugiuchi teaches a method of quantitating LDL cholesterol with a reagent composition containing cholesterol dehydrogenase, cholesterol esterase and oxidized coenzyme (NAD) wherein reduced coenzyme is measured (Column 20, Claim 1 and Column 10, Lines 11-12).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of determining total and LDL cholesterol as taught by Shull *et al.* with the method of determining LDL cholesterol of Sugiuchi because both techniques utilize similar methods to enzymatically determine LDL cholesterol.

One of ordinary skill in the art would have recognized that the two references teach alternate means of arriving at the same conclusion, the amount of LDL cholesterol and the choice of enzymatic pathway would have been dependent upon artisan preference. There would have been a reasonable expectation of success in making this combination because Sugiuchi teaches cholesterol determination by both pathways and enzyme combinations.

Claims1, 13-15 and 20-24 are newly rejected under 35 U.S.C. §103(a) as being unpatentable over Shull *et al.* (US 2004/0126830 A1) in view of Kishi *et al.* (US 2003/0129681 A1).

The teachings of Shull *et al.* were discussed above.

Shull *et al.* does not teach a method wherein the first step is carried out in the presence of lipoprotein lipase.

Kishi *et al.* teaches a method of determining VLDL comprising the use of albumin and lipoprotein lipase and wherein albumin is added to suppress the reactivity of LPL with HDL (Pg. 2, Paragraph [0015]).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of determining total and LDL cholesterol as taught by Shull *et al.* with the method of determining VLDL cholesterol of Kishi *et al.* because both methods are drawn to similar methods of enzymatic determination of specific lipoproteins. One of ordinary skill in the art would have recognized that lipoprotein lipase is a functional equivalent of the cholesterol esterase of Shull *et al.* both of which hydrolyze lipoprotein to release the components therein. There would have been a reasonable expectation of success in making this modification because both methods are drawn to the use of similar methods and reagents in the quantitative determination of lipoproteins.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL C. MARTIN whose telephone number is (571)272-3348. The examiner can normally be reached on M-F 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

02/13/08

/Jon P Weber/

Supervisory Patent Examiner, Art Unit 1657